UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/986,191	11/07/2001	Jian Ni	PF256D1C1	4926

22195 7590 07/06/2005

HUMAN GENOME SCIENCES INC
INTELLECTUAL PROPERTY DEPT.
14200 SHADY GROVE ROAD
ROCKVILLE, MD 20850

EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/986,191	NI ET AL.	
	Examiner	Art Unit	
	Joseph F. Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 23-54 are pending and under consideration.

Response to Amendment

Applicant's arguments filed 5/5/2005 have been fully considered but they are persuasive in part.

The rejection of claims 41-54 under 35 USC 112 first paragraph, insofar as they lack enablement for fragments of the polypeptide, has been withdrawn based on Applicant's arguments.

Remaining issues are set forth below.

Claim Rejections - 35 USC §§ 101, 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-54 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility, for reasons of record set forth in the Office Action of 2/8/2005. The instant application has provided a description of a protein. The instant application does not disclose the biological role of this protein or its significance. Applicant is

directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

The rejection of record set forth that the CCIII is homologous to known proteins. However, it is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors (Doerks et al.1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved (Doerks et al. page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods have led to significant function-annotation errors in the sequence databases (Doerks et al. page 250, column 1, third paragraph). Furthermore, Brenner (1999, Trends in Genetics 15:334-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

After complete characterization, this protein may be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson,* 148 USPQ 689 (Sup. Ct., 1966), in

which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 USC § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a polypeptide that has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as CCIII, the instant invention is incomplete. In the absence of knowledge of the natural substrate or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances that inhibit its activity is clearly to use it as the object of further research that has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for CCIII then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 USC § 101 as being useful.

Applicant has provided two references regarding the utility of the claimed polypeptide. The Chien and Pei reference discloses a polynucleotide which encodes the CCIII polypeptide of the present invention and identify this polynucleotide as PTTG binding factor (PBF)". See, page 19423. Chien and Pei demonstrate that PBF binds directly to Pituitary tumor-transforming gene PTTG, a polypeptide believed responsible for tumorigenesis in the pituitary and various other tissues. See, page 19422 and Figures 3-5 at pages 19423-19424. Chien and Pei further demonstrated that PBF binding is required for PTTG activation of transcription from the bFGF promoter. Furthermore, McCabe et al. demonstrate that expression of PBF was up-regulated six-fold in pituitary tumors isolated from a large cohort of patients. See, Exhibit B at page 144, right column first paragraph; and page 145, Figure 2. McCabe et al. determined their data support a fundamental role for PTTG-mediated up-regulation of FGF-2 signaling in pituitary tumorigenesis." See, Exhibit A at page 141, right column lines 7-9. Because the polypeptide identified by McCabe et al. as PBF is identical to CCIII of the present invention, because the polypeptide identified by McCabe et al. as ETBF" is up-regulated in pituitary tumors, and because the polypeptide identified by McCabe et al. as PBF is required for P'I'TG activation of FGF transcription, the observations described above confirm Applicants' assertion of a specific utility that the CCIII polypeptides, antibodies and polynucleotides of the present invention will be useful in the diagnosis of cancers and tumors.

According to MPEP 2107, in order for Applicant to rebut the rejection for lack of utility imposed because the invention lacks an asserted specific and substantial utility for the claimed invention and it does not have a readily apparent well-established utility, Applicant must provide evidence that one of ordinary skill in the art would have recognized that the identified specific

and substantial utility was well-established at the time of filing. The examiner should also ensure that there is an adequate nexus between the evidence and the properties of the now claimed subject matter as disclosed in the application as filed. That is, the applicant has the burden to establish a probative relation between the submitted evidence and the originally disclosed properties of the claimed invention.

In the instant case, the filing date of the Application is 11/7/2001, with an effective filing date of 3/5/1996. The Chien and Pei reference has a publication date of June 23, 2000, while the McCabe reference was published in 2003. Thus, these references which establish the function of CCIII as a binding protein which activates transcription of PTTG are post-filing, and as such, do not provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established at the time of filing. At the time of filing the function of the CCIII polypeptide was not known, nor were any specific disease associations known, and these references do not show that the CCIII polypeptide had a well-established utility at the time of filing. Additionally, the McCabe reference teaches that PBF (CCIII) has not previously been described in pituitary tumors, and that for the first time they demonstrated that PTTG mRNA expression is positively associated with that of its binding factor, and that PBF (CCIII) is significantly raised in tumors (McCabe at 149, column 1, second paragraph), thus establishing that one of ordinary skill in the art would not have recognized that the identified specific and substantial utility was well-established at the time of filing.

Additionally, there is not an adequate nexus between the evidence and the properties of the now claimed subject matter as disclosed in the application as filed. The Speciation is silent with regards to the subsequently discovered function of the CCIII polypeptide as a binding

factor. Furthermore, there is no indication that the CCIII polypeptide could serve as a marker for pituitary tumors, only that it could be used to detect "neoplasia" (Specification at 34, paragraph 171). The only indication as to the disorders for which the CCIII protein could be used as a diagnostic is a list on page 4 of the Specification (paragraph 22) from which the skilled artisan would need to pick out one of the disorders and determine the role of the CCIII polypeptide in the disorder (if it had one). Clearly, this would not be a well-established utility, given the teaching of McCabe that the role of CCIII (which McCabe refers to as "PBF") was not known before 2003. Since, the specification did not disclose a specific role that CCIII may play in a specific disease, but rather, broadly contemplated a possible role in a disparate listing of many diseases, thus not providing sufficient evidence that a specific and substantial utility based on an association and role in any disease process was known at the time of filing.

Claims 23-54 stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

Claims 23-54 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.
Primary Examiner
Art Unit 1646
June 28, 2005

JOSEPH MURPHY
PATENT EXAMINER